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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,475	10/10/2001	Ryuichi Morishita	6235-59221	4309

24197 7590 01/13/2004

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EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 01/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/869,475	MORISHITA ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8/18/03*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9,11,12 and 14-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9,11,12 and 14-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8/18/03* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Final Rejection

Claims 9, 11, 12, and 14-16 are pending examination.

Applicants' traversal filed on 8/18/03 and the Declaration filed under 1.132 by Dr. Morishita filed on 9/5/03 is acknowledged and considered.

Election/Restrictions

This application contains species in claim 11 drawn to species nonelected with traverse in Paper No. filed on 7/2/02. A complete reply to the final rejection must include cancellation of nonelected species or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the

reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 9, 11, 12, and 14-16 remain rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Morishita et al. (US 6,248,722) in view of Gene Therapy of Osaka University, English translation from the Japan Financial News Paper, Local News Section (Dec. 14, 1998) (IDS). Morishita teaches a method of nucleic acid therapy for treating a disease in a subject for which hepatocyte growth factor (HGF) is effective, comprising administering to the muscle of the subject a HVJ-liposome comprising HGF (column 14). Morishita teaches that HGF can treat arterial diseases (column 4, lines 35-49). Morishita further teaches that the HGF gene in the method may be appropriately varied depending upon the disease to be treated in a dose 0.0001mg to 100 mg, preferably 0.001mg to 10 mg (column 6, lines 48-54), which anticipates administering at least 50μg of the nucleic acid encoding HGF. Furthermore, Morishita teaches that the dose may be divided into several days or few months, which would anticipate delivering the nucleic acid several times to the subject (column 6, lines 53-54). The pathology of an ischemic disease in a subject results in poor circulation in an affected area (e.g. lower limb, heart, brain) of the subject. HGF gene therapy results in increase circulation of blood in the affected area of the subject. The art of record indicates that there are only a few types of ischemic diseases. Thus, one skilled in the art would have anticipated that using HGF gene therapy to treat an ischemic disease in a subject taught by Morishita would embrace treating diabetic ischemic disease in the lower limb of a subject with the disease.

In addition, Gene Therapy of Osaka University, English translation from the Japan Financial News Paper, Local News Section teaches that arteriosclerosis bitterns is a lower limb

arteriosclerosis caused by diabetes mellitus resulting in the aggravation in blood circulation followed by lower limb necrosis or gangrene. A scientist, Dr. Ogihara, was cited in the Japan Financial News Paper, Local News Section and he states that, "the HGF has a more potent angiogenesis activity and less side effects than VEGF." Gene Therapy of Osaka University, English translation from the Japan Financial News Paper, Local News Section further teaches that, "a gene encoding the HGF having angiogenesis activity is introduced into a special circular gene, a plasmid, followed by injection to a muscle around the affected part in the patient." Thus, one of ordinary skill in the art would have been motivated as obvious over Morishita in view of Gene Therapy of Osaka University, English translation from the Japan Financial News Paper, Local News Section (Dec. 14, 1998) to treat diabetic lower limb ischemic disease in a subject using HGF nucleic acid therapy since diabetic lower limb ischemic disease results in lower limb arteriosclerosis and HGF gene therapy can be used to regenerate new vasculars in an affected of the subject.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Applicant's arguments filed 8/18/03 have been fully considered but they are not persuasive because of the reasons set forth under the 102(e) rejection.

With respect to applicants' arguments that, "'722 patent does not disclose the treatment of diabetic ischemic disease, it cannot anticipate claims 9, 11, 12, or 14-16 (See pages 4-5)," the argument is not found persuasive because while it is acknowledged that '722 patent by itself does not specifically anticipate treating lower ischemic diabetes in a subject using HGF, the examiner used the '722 in a 102/103 rejection in view of the art of record indicating that there are only a few types of ischemic diseases. Thus, one skilled in the art would have anticipated that using HGF gene therapy to treat an ischemic disease in a subject taught by Morishita would embrace treating diabetic ischemic disease in the lower limb of a subject with the disease.

In addition, Applicants' arguments are solely directed to the '722 patent and do not address the Gene Therapy of Osaka University, English translation from the Japan Financial News Paper, Local News Section (Dec. 14, 1998) reference in their argument.

In view of the secondary reference, one of ordinary skill in the art would have been motivated in view of Morishita as obvious over Gene Therapy of Osaka University, English translation from the Japan Financial News Paper, Local News Section (Dec. 14, 1998) to treat diabetic lower limb ischemic disease in a subject using HGF nucleic acid therapy since diabetic lower limb ischemic disease results in lower limb arteriosclerosis and HGF gene therapy can be used to regenerate new blood vessels in an affected of the subject.

Applicants have not provided a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Furthermore, the assertion that, "it was not known, nor would it be obvious, to administer HGF to a patient with diabetic ischemic disease (page 5)," is not found persuasive because other

than the applicants' assertion, the applicants provide no guidance or factual evidence to support the assertion. See MPEP § 716.01(c).

Claims 9, 11, 12, 15, and 16 remain rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Isner (US 6,121,246) in view of Gene Therapy of Osaka University, English translation from the Japan Financial News Paper, Local News Section (Dec. 14, 1998) (IDS). Isner teaches a method of treating ischemic tissue in a mammal, which comprises injecting into the tissue a nucleic acid capable of expressing an angiogenic protein, wherein the nucleic acid encodes a hepatocyte growth factor and wherein the amount of nucleic acid injected is 500μg (column 14). Isner teaches that the nucleic acid can be injected at multiple sites throughout the ischemic tissue that would anticipate administering the nucleic acid repeatedly (column 6, lines 27-28). The pathology of an ischemic disease in a subject results in poor circulation in an affected area (e.g. lower limb, heart, brain) of the subject. The art of record indicates that there are only a few types of ischemic diseases. HGF gene therapy results in increase circulation of blood in the affected area of the subject. Thus, one skilled in the art would have anticipated that using HGF gene therapy to treat an ischemic disease in a subject taught by Isner would embrace treating diabetic ischemic disease in the lower limb of a subject with the disease.

In addition, Gene Therapy of Osaka University, English translation from the Japan Financial News Paper, Local News Section teaches that arteriosclerosis bitterns is a lower limb arteriosclerosis caused by diabetes mellitus resulting in the aggravation in blood circulation followed by lower limb necrosis or gangrene. A scientist, Dr. Ogihara, is cited in the Japan

Financial News Paper, Local News Section and he states that, "the HGF has a more potent angiogenesis activity and less side effects than VEGF." Gene Therapy of Osaka University, English translation from the Japan Financial News Paper, Local News Section further teaches that, "a gene encoding the HGF having angiogenesis activity is introduced into a special circular gene, a plasmid, followed by injection to a muscle around the affected part in the patient." Thus, one of ordinary skill in the art would have been motivated in view of Isner as obvious over Gene Therapy of Osaka University, English translation from the Japan Financial News Paper, Local News Section (Dec. 14, 1998) to treat diabetic lower limb ischemic disease in a subject using HGF nucleic acid therapy since diabetic lower limb ischemic disease results in lower limb arteriosclerosis and HGF gene therapy can be used to regenerate new vasculars in an affected of the subject.

Applicant's arguments filed 8/18/03 have been fully considered but they are not persuasive because of the reasons set forth under the 102(e) rejection.

With respect to applicants' arguments that, "the '246 patent does not render obvious use of HGF" and "In addition, the amount of HGF of use is considerably less than the amount of VEGF of use. Specifically, the use of 50 μg of a nucleic acid encoding HGF is effective, only one tenth the amount of nucleic acid encoding VEGF (see page 6)," the argument is not found persuasive because the feature upon which applicant relies (i.e., 50 μg of a nucleic acid encoding HGF) is not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9 and 14 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Isner (US 6,121,246) taken with Gene Therapy of Osaka University, English translation from the Japan Financial News Paper, Local News Section (Dec. 14, 1998) (IDS) in further view of Afione et al. (IDS, Clin. Pharmacokinet 28: 181-189, 1995).

Isner teaches a method of treating ischemic tissue in a mammal, which comprises injecting into the tissue a nucleic acid capable of expressing an angiogenic protein, wherein the nucleic acid encodes a hepatocyte growth factor and wherein the amount of nucleic acid injected is 500μg (column 14). Isner teaches that the nucleic acid can be injected at multiple sites throughout the ischemic tissue that would anticipate administering the nucleic acid repeatedly (column 6, lines 27-28). The pathology of an ischemic disease in a subject results in poor circulation in an affected area (e.g. lower limb, heart, brain) of the subject. The art of record indicates that there are only a few types of ischemic diseases. HGF gene therapy results in increase circulation of blood in a subject that has an area with poor circulation of blood. In addition, Gene Therapy of Osaka University, English translation from the Japan Financial News Paper, Local News Section teaches that arteriosclerosis bitterns is a lower limb arteriosclerosis caused by diabetes mellitus resulting in the aggravation in blood circulation followed by lower limb necrosis or gangrene. A scientist, Dr. Ogihara, is cited in the Japan Financial News Paper, Local News Section and he states that, "the HGF has a more potent angiogenesis activity and less side effects than VEGF." Gene Therapy of Osaka University, English translation from the Japan Financial News Paper, Local News Section further teaches that, "a gene encoding the HGF having angiogenesis activity is introduced into a special circular gene, a plasmid, followed by injection to a muscle around the affected part in the patient." Thus, one skilled in the art would have anticipated that using HGF gene therapy to treat an ischemic disease in a subject taught by Isner would embrace treating diabetic ischemic disease in the lower limb of a subject with the disease. However, Isner does not specifically teach administering the nucleic acid encoding the HGF in the form of HVJ-liposome.

However, at the time the invention was made, HVJ-liposome was known in the art for delivering a nucleic acid to a cell in a mammal as exemplified by Afione. Afione teaches that HVJ-liposome technology can be used to facilitate nuclear translocation and deter lysosomal degradation (page 185).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to use HVJ-liposome comprising a nucleic acid encoding HGF in a method of treating lower limb diabetic ischemic disease in a subject. One of ordinary skill in the art would have been motivated to use HVJ-liposome to deliver a nucleic acid encoding HGF to a subject because the HVJ-liposome can improve nucleic acid expression by deterring lysosomal degradation of the nucleic acid.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicants' arguments filed 8/18/03 have been fully considered but they are not persuasive for the following reasons:

The Declaration under 37 CFR 1.132 filed 9/5/03 is insufficient to overcome the rejection of claim 9 and 14 based upon 103(a) as set forth in the last Office action because: the Declaration cannot be used to overcome a prior art rejection based on a 102(b) reference. The statement that, "the article was published less than one year before the priority application Japanese Patent Application No. 11/309984, was filed is incorrect." The priority date is 10/26/00 of the pending application and not 10/29/99. Thus, the Japanese newspaper article was published more than 1 year from the US filing date 10/26/00 and the article is a 102(b) reference and not a 102(a)

reference. See MPEP 706.02, DETERMINING THE EFFECTIVE FILING DATE OF THE APPLICATION.

Furthermore applicants' statement, "claims 9, 11, 12, and 15-16 are rejected as being obvious over Gene Therapy Osaka University, English translation from the Japan Financial Local News Section (December 14, 1998)," is incorrect because only claims 9 and 14 were rejected in the 103(a) rejection.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775.

The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, acting SPE - Art Unit 1635, can be reached at (703) 306-3217.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER

Brian Whiteman
Patent Examiner, Group 1635